

## **REMARKS**

### **Terminal Disclaimer**

The Office Action rejection claim 50 under the doctrine of obviousness-type double patenting relative to U.S. Patent No. 6,226,352. Without agreeing to this rejection or admitting that this rejection is proper, Applicant is providing a terminal disclaimer, relative to U.S. Patent No. 6,226,352. Thus, the rejection should be removed.

### **Rejection of Claim 50 under 35 U.S.C. 112, second paragraph**

Claim 50 was rejected under 35 U.S.C. 112, second paragraph. The claim has been amended to recited the limitations with greater clarity.

### **Rejection of Claim 50 under 35 U.S.C. 102(b) over Bertoni (US 4,455,292)**

Claim 50 stands rejected under 35 U.S.C. 102(b) as being anticipated by Bertoni (US 4,455,292) on the grounds that “the cited reference discloses radiocontrast agent iodo-benzamidoglucopyranose such as metrizamide (column 2, lines 34+)”.

MPEP 2131 sets out the requirements for a rejection of a claim under 35 U.S.C 102.

To anticipate a claim the reference must teach every element of the claim. A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Amended claim 50 recites the limitation of a compound having an S moiety that binds to an intracellular target. The specification (page 9, line 17 – page 10, line 11) discloses that the prior art in radiography teaches contrast agents that function by passively outline body structures and organs, and which accumulate interstitially in the extracellular space. The contrast agents of the prior are designed to be hydrophilic, and are not cell membrane-permeable.

The log P parameter is the standard measure of the hydrophilicity or hydrophobicity of a compound. The specification discloses that for compounds such as radiographic contrast agents

having molecular weights of equal to or less than about 1000 Da, a log P value of greater than about 0.0 is a prerequisite for cell membrane permeability (page 29, line 22 – page 30, line 2).

Table 1 of the specification (page 30, lines 10 – 20) compares the log P values of metrizamide, the contrast agent disclosed by Bertoni, and other widely used contrast agents of the prior art with the log P values of exemplary imaging agents of the instant claims. The contrast agents of the prior art have log P values of less than 0.0, while the imaging agents of the instant claims have log P values of greater than about 0.0. Applicant submits that amended claim 50 is not anticipated by Bertoni, in that the cited reference fails to teach or suggest each of the limitations recited by the claim.

#### **Rejection of Claim 50 under 35 U.S.C. 102(b) over Chien et al.**

Claim 50 was also rejected under 35 U.S.C. 102(b) as being anticipated by Chien et al. The reference teaches the use of [<sup>125</sup>I] - *p*-phenylpentadecanoic acid in radiopharmaceutical-based imaging studies of cardiac metabolism. Claim 50 recites the limitation of an S moiety selected from pyranose and furanose. Chien et al. neither teaches nor suggests a compound comprising a pyranose or furanose moiety. Applicant submits that claim 50 is not anticipated by Chien et al., in that the reference fails to meet each of the limitations recited by the claim.

#### **Rejection of Claim 50 Under 35 U.S.C. 103(a) as Obvious over Shefer (US 4,887,604) in view of Bertoni (US 4,455,292), and Obvious over Shefer in view of Sovak (US 4,243,653).**

Claim 50 was rejected under 35 U.S.C. 103(a) as being obvious over Shefer et al. (US 4,887,604) in view of Bertoni (US 4,455,292), and obvious over Shefer et al. in view of Sovak et al. (US 4,243,653).

Shefer et al. discloses a dual energy radiographic imaging system for diagnostic applications such as angiography. The reference fails to identify any specific contrast agents by name or chemical structure, and specifically discloses only that the radio-opacifying element of the contrast agent is iodine. The reference fails to teach or suggest a contrast agent that is cell membrane-permeable.

As previously noted, Bertoni discloses metrizamide, a contrast agent which is hydrophilic and therefore unable to permeate the cell membrane. A contrast agent resulting

from the proposed combination of Bertoni with Shefer et al. thus fails to meet the requirement of amended claim 50 of an imaging agent that binds to an intracellular target.

Similarly, a contrast agent resulting from the combined teachings of Shefer et al and Sovak would be hydrophilic, unable to permeate the plasma membrane, and thus incapable of binding to an intracellular target. Sovak et al. teaches the desirability of contrast agents that are strongly hydrophilic, because increased hydrophilicity improves water solubility. Sovak et al. neither teaches nor suggests contrast agents that are cell membrane-permeable. The contrast agent of the proposed combination of references thus fails to meet the limitation recited by amended claim 50 of a S moiety that binds to an intracellular target. Applicant submits that as amended, claim 50 is unobvious over the combination of Shefer et al. and Sovak et al., in that the proposed combination of references fails to meet each of the limitations of amended claim 50.

#### **Request for Extension of Time**

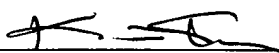
Applicant respectfully requests an extension of time to respond to the pending Office Action and a check for the necessary extension fee is enclosed herewith.

Please charge any shortages or credit any overages to Deposit Account No. 02-2666.

Respectfully submitted,

BLAKELY, SOKOLOFF, TAYLOR & ZAFMAN

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